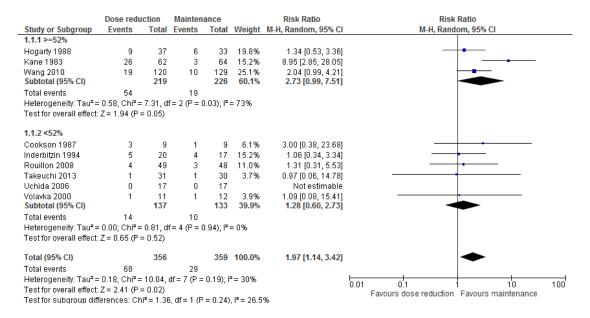
Supplementary Figure S7. Forest plot: Subgroup analysis, factors related to antipsychotic use and dose reduction strategy

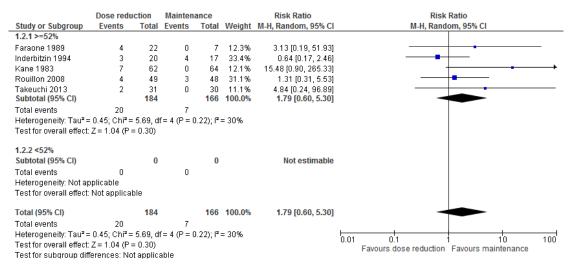
D. Actual proportion of reduction

1. Relapse/Hospitalization

1.1 Relapse (primary outcome)

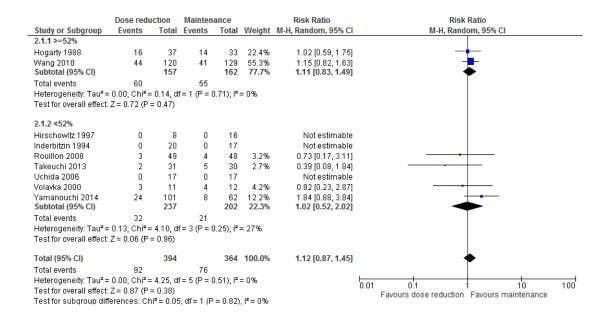


1.2 Hospitalization

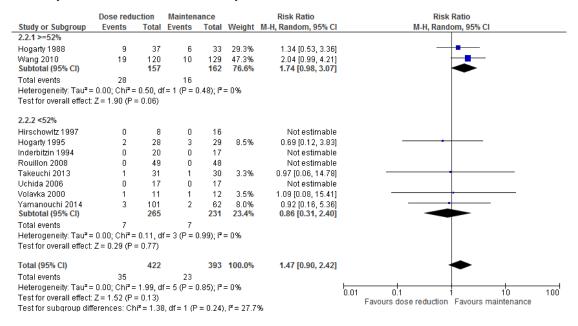


2. Study discontinuation

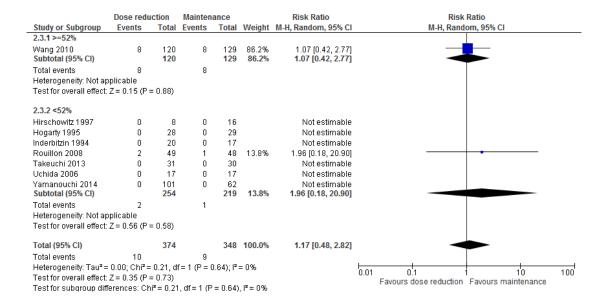
2.1 Study discontinuation due to all causes



2.2 Study discontinuation due to inefficacy

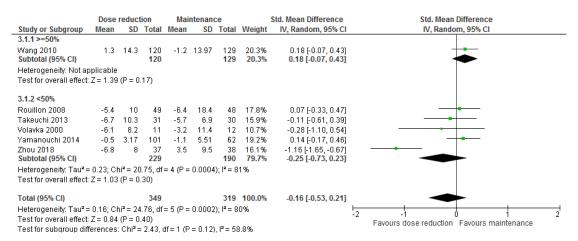


2.3 Study discontinuation due to intolerability

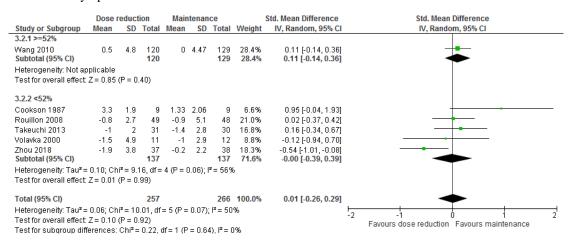


3. Psychopathology

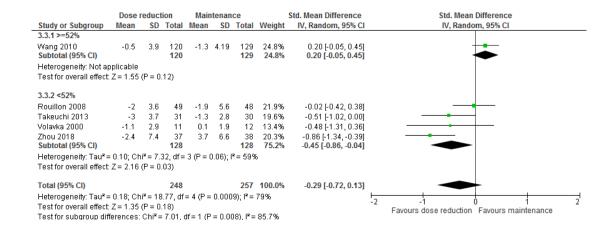
3.1 Total



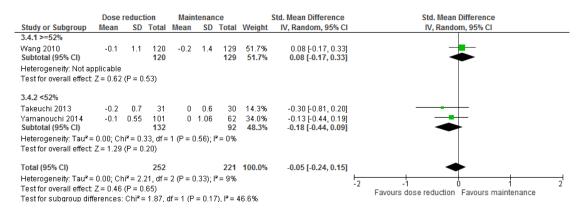
3.2 Positive symptoms



3.3 Negative symptoms

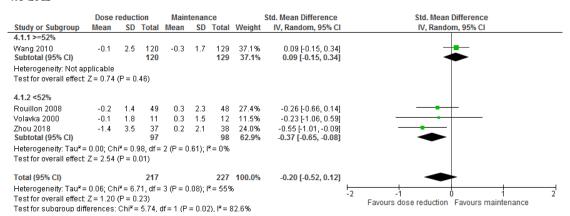


3.4 CGI-S



4. Adverse effects

4.1 SAS



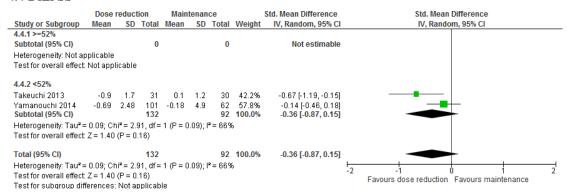
4.2 BARS

	Dose	reduct	tion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 >=52%									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not a	pplicable								
Test for overall effect	: Not app	licable							
4.2.2 <52%									
Rouillon 2008	0.02	1.2	49	-0.04	1.6	48	100.0%	0.04 [-0.36, 0.44]	
Subtotal (95% CI)			49			48	100.0%	0.04 [-0.36, 0.44]	-
Heterogeneity: Not a	pplicable								
Test for overall effect	Z = 0.21	(P = 0	.84)						
Total (95% CI)			49			48	100.0%	0.04 [-0.36, 0.44]	-
Heterogeneity: Not a	pplicable								-2 -1 1 2
Test for overall effect	Z = 0.21	(P = 0)	.84)						Favours dose reduction Favours maintenance
Test for subgroup differences: Not applicable									rayours dose reduction rayours maintenance

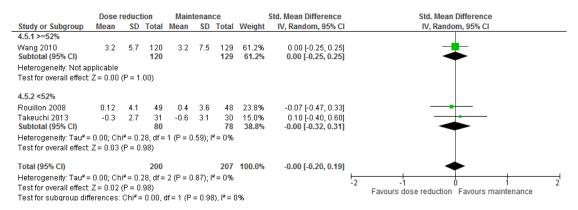
4.3 AIMS

Dose	reduct	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
		0			0		Not estimable	
plicable								
Not appl	icable							
-0.1	1.6	49	-0.4	1.7	48	100.0%	0.18 [-0.22, 0.58]	
		49			48	100.0%	0.18 [-0.22, 0.58]	
plicable								
Z = 0.89	(P = 0	.38)						
		49			48	100.0%	0.18 [-0.22, 0.58]	-
plicable								-2 -1 1 2
Z = 0.89	(P = 0)	.38)						-2 -1 U 1 2 Favours dose reduction Favours maintenance
erences:	Not a	pplicab	le					r avours dose reduction. Favours maintenance
	plicable Not appl -0.1 plicable Z = 0.89 plicable Z = 0.89	Mean SD plicable Not applicable -0.1 1.6 plicable $Z = 0.89 (P = 0)$ plicable $Z = 0.89 (P = 0)$	0 plicable Not applicable -0.1 1.6 49 49 plicable Z = 0.89 (P = 0.38) 49 plicable Z = 0.89 (P = 0.38)	Mean SD Total Mean oplicable Not applicable 0 49 -0.4 -0.1 1.6 49 -0.4 plicable Z = 0.89 (P = 0.38) 49 49 plicable 49 10.4	Mean SD Total Mean SD 0 plicable -0.1 1.6 49 -0.4 1.7 plicable Z = 0.89 (P = 0.38) 49 plicable Z = 0.89 (P = 0.38) 49	Mean SD Total Mean SD Total 0 0 0 0 0 0 1.6 49 -0.4 1.7 48 48 plicable Z = 0.89 (P = 0.38)	Note	Not estimable Not applicable Not applicable Yes Not estimable Not applicable Not applicable Yes Not estimable Not estim

4.4 DIEPSS



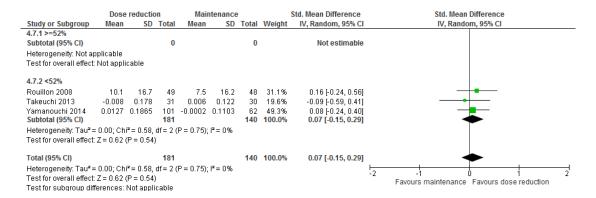
4.5 Body weight



4.6 Neurocognition

	Dose	Dose reduction Maintenance						Std. Mean Difference		Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI			
4.6.1 >=52%													
Subtotal (95% CI)			0			0		Not estimable					
Heterogeneity: Not a	pplicable	!											
Test for overall effect	t: Not app	licable											
4.6.2 < 52%													
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]					
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]					
Subtotal (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]					
Heterogeneity: Tau2:	= 0.03; C	hi² = 1.	52, df=	1 (P =	0.22); I	r = 349	6						
Test for overall effect	t: Z = 3.12	P = 0	.002)										
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]					
Heterogeneity: Tau ² :	= 0.03; C	hi² = 1.	52, df=	1 (P =	0.22); (²= 349	6		-2	<u> </u>			
Test for overall effect	t: Z = 3.12	(P = 0	.002)						-2	Favours maintenance Favours dose reduction			
Test for subgroup di	up differences: Not applicable									i avours maintenance i avours dose reduction			

4.7 QOL

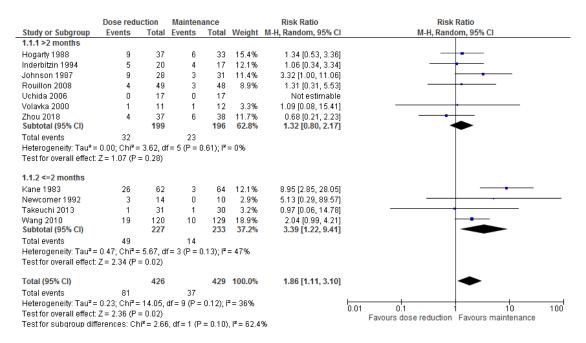


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale

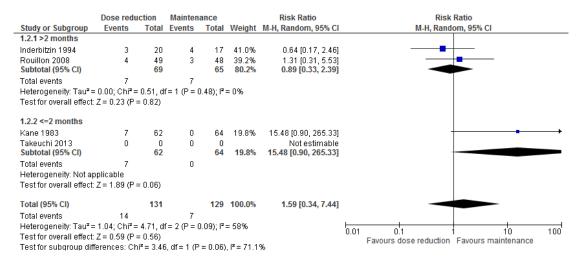
E. Duration of reduction

1. Relapse/Hospitalization

1.1 Relapse (primary outcome)

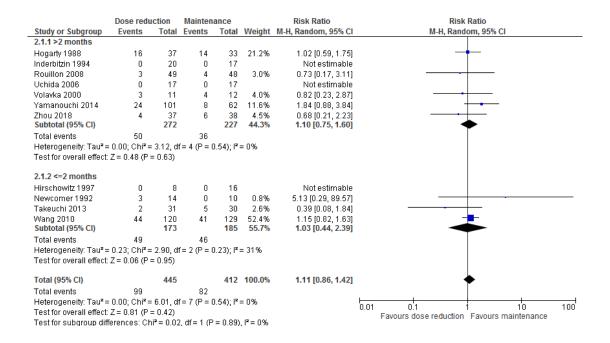


1.2 Hospitalization

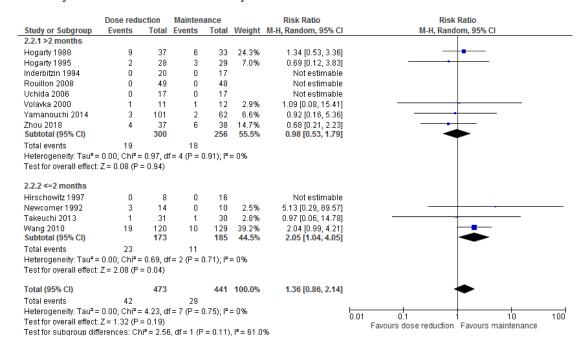


2. Study discontinuation

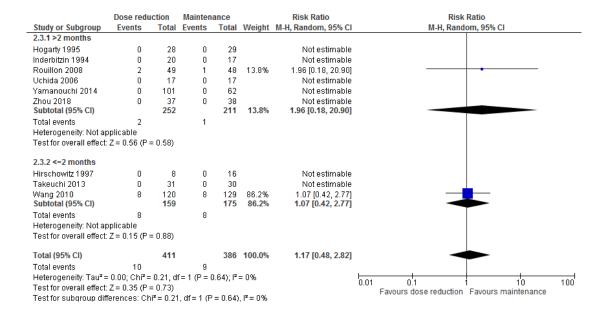
2.1 Study discontinuation due to all causes



2.2 Study discontinuation due to inefficacy

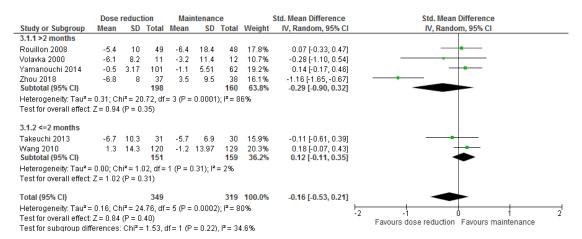


2.3 Study discontinuation due to intolerability

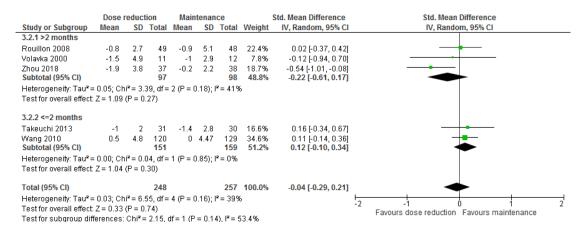


3. Psychopathology

3.1 Total



3.2 Positive symptoms



3.3 Negative symptoms

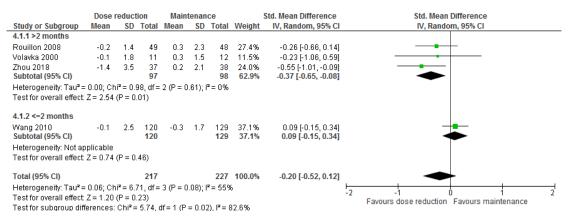
	Dose	reduct	ion	Main	itenan	ce		Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
3.3.1 >2 months												
Rouillon 2008	-2	3.6	49	-1.9	5.6	48	21.9%	-0.02 [-0.42, 0.38]				
Volavka 2000	-1.1	2.9	11	0.1	1.9	12	13.4%	-0.48 [-1.31, 0.36]				
Zhou 2018 Subtotal (95% CI)	-2.4	7.4	37 97	3.7	6.6	38 98	20.3% 55.7%	-0.86 [-1.34, -0.39] - 0.44 [-1.02, 0.15]				
Heterogeneity: Tau ^z : Test for overall effect				2 (P = 1	0.03); I	²= 72%	6					
3.3.2 <=2 months												
Takeuchi 2013	-3	3.7	31	-1.3	2.8	30	19.6%	-0.51 [-1.02, 0.00]				
Wang 2010 Subtotal (95% CI)	-0.5	3.9	120 151	-1.3	4.19	129 159	24.8% 44.3%	0.20 [-0.05, 0.45] -0.12 [-0.81, 0.57]				
Heterogeneity: Tau ² : Test for overall effect				1 (P = 1	0.01); I	²= 83%	6					
Total (95% CI)			248			257	100.0%	-0.29 [-0.72, 0.13]				
Heterogeneity: Tau ² : Test for overall effect Test for subgroup di	: Z = 1.35	(P = 0.	18)						-2 -1 0 1 2 Favours dose reduction Favours maintenance			

3.4 CGI-S

	Dose	reduct	tion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.4.1 > 2 months									
Yamanouchi 2014	-0.1	0.55	101	0	1.06	62	34.0%	-0.13 [-0.44, 0.19]	
Subtotal (95% CI)			101			62	34.0%	-0.13 [-0.44, 0.19]	-
Heterogeneity: Not a	pplicable								
Test for overall effect	Z = 0.79	(P = 0	.43)						
3.4.2 <= 2 months									
Takeuchi 2013	-0.2	0.7	31	0	0.6	30	14.3%	-0.30 [-0.81, 0.20]	
Wang 2010	-0.1	1.1	120	-0.2	1.4	129	51.7%	0.08 [-0.17, 0.33]	-
Subtotal (95% CI)			151			159	66.0%	-0.05 [-0.40, 0.30]	-
Heterogeneity: Tau ² =	= 0.03; CI	hi² = 1.	76, df=	1 (P = 0)	0.18); I	2 = 439	6		
Test for overall effect	Z = 0.26	(P = 0	.80)						
Total (95% CI)			252			221	100.0%	-0.05 [-0.24, 0.15]	•
Heterogeneity: Tau ² =	= 0.00; CI	hi² = 2.:	21, df=	2 (P = 0	0.33); [²=9%			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Test for overall effect	Z = 0.46	(P = 0	.65)	-					-2 -1 0 1 2 Favours dose reduction Favours maintenance
Test for subgroup dif	ferences	: Chi²=	0.11.	df = 1 (P	= 0.74	4), $I^2 = 0$	0%		ravours dose reduction Favours maintenance

4. Adverse effects

4.1 SAS



4.2 BARS

	Dose reduction				ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD To	tal Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 >2 months								
Rouillon 2008 Subtotal (95% CI)	0.02		49 -0.04 49	1.6	48 48		0.04 [-0.36, 0.44] 0.04 [-0.36, 0.44]	
Heterogeneity: Not app	plicable							
Test for overall effect: 2	Z = 0.21 ((P = 0.84)						
4.2.2 <=2 months								
Subtotal (95% CI)			0		0		Not estimable	
Heterogeneity: Not app	olicable							
Test for overall effect: I	Not appli	cable						
Total (95% CI)			49		48	100.0%	0.04 [-0.36, 0.44]	
Heterogeneity: Not app	olicable							
Test for overall effect: 2		P = 0.84						-2 -1 0 1 2
Test for subgroup diffe								Favours dose reduction Favours maintenance

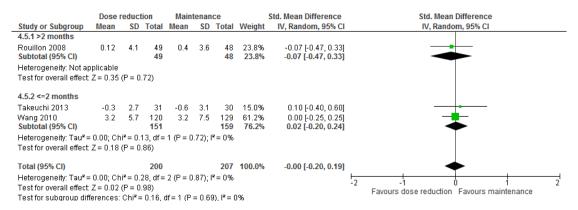
4.3 AIMS

	Dose r	educt	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.3.1 >2 months									
Rouillon 2008	-0.1	1.6	49	-0.4	1.7	48	100.0%	0.18 [-0.22, 0.58]	
Subtotal (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	
Heterogeneity: Not app	olicable								
Test for overall effect: 2	Z = 0.89 (P = 0.	38)						
4.3.2 <= 2 months									
Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not app	olicable								
Test for overall effect: N	Not appli	cable							
Total (95% CI)			49			48	100.0%	0.18 [-0.22, 0.58]	
Heterogeneity: Not app	olicable								
Test for overall effect: Z		P = 0.	38)						-2 -1 0 1 2
Test for subgroup diffe		•		le					Favours dose reduction Favours maintenance

4.4 DIEPSS

	Dose	reduct	ion	Main	tenan	ce		Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
4.4.1 >2 months												
Yamanouchi 2014 Subtotal (95% CI)	-0.69	2.48	101 101	-0.18	4.9	62 62	57.8% 57.8%	-0.14 [-0.46, 0.18] - 0.14 [-0.46, 0.18]				
Heterogeneity: Not a	pplicable											
Test for overall effect	Z= 0.87	(P = 0	.38)									
4.4.2 <= 2 months												
Takeuchi 2013	-0.9	1.7	31	0.1	1.2	30	42.2%	-0.67 [-1.19, -0.15]				
Subtotal (95% CI)			31			30	42.2%	-0.67 [-1.19, -0.15]				
Heterogeneity: Not ap	pplicable											
Test for overall effect	: Z= 2.54	(P = 0	.01)									
Total (95% CI)			132			92	100.0%	-0.36 [-0.87, 0.15]				
Heterogeneity: Tau ² =	= 0.09; Ct	ni² = 2.9	91, df=	1 (P = 0)	1.09); [² = 669	5		-2 -1	<u>ا</u>		
Test for overall effect	Z = 1.40	(P = 0)	.16)				Favours dose reduction Favours maintenance	-				
Test for subgroup dif	ferences	: Chi²=	2.91, (df = 1 (P	= 0.09	$3), 1^2 = 6$	55.7%		1 avours dose reduction 1 avours maintenance			

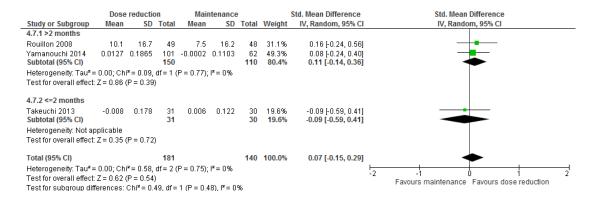
4.5 Body weight



4.6 Neurocognition

	Dose reduction				itenan	ce		Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
4.6.1 > 2 months												
Zhou 2018 Subtotal (95% CI)	9.8	13.7	37 37	3.6	11.5	38 38	54.6% 54.6%	0.49 [0.03, 0.95] 0.49 [0.03, 0.95]				
Heterogeneity: Not as	oplicable											
Test for overall effect	Z= 2.07	(P = 0)	.04)									
4.6.2 <= 2 months												
Takeuchi 2013 Subtotal (95% CI)	7	7.1	31 31	-0.1	8	30 30	45.4% 45.4 %	0.93 [0.40, 1.46] 0.93 [0.40, 1.46]				
Heterogeneity: Not a	oplicable											
Test for overall effect	Z= 3.43	(P = 0)	.0006)									
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	-			
Heterogeneity: Tau ² =	= 0.03; CH	ni² = 1.:	52. df=	1 (P = I	0.22): I	² = 349		+ 				
Test for overall effect				•	-71				-2 -1 0 1			
Test for subgroup dif		,		df = 1 (P		Favours maintenance Favours dose reduction						

4.7 QOL

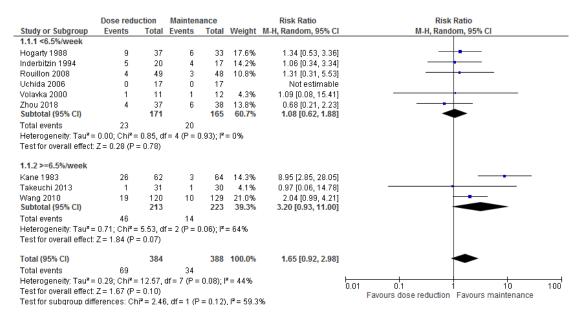


Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale

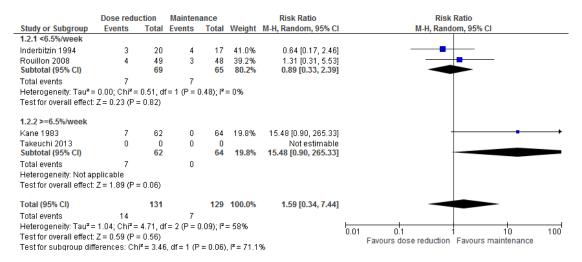
F. Speed of reduction

1. Relapse/Hospitalization

1.1 Relapse (primary outcome)

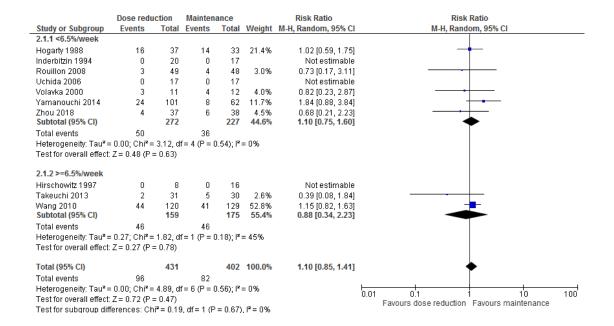


1.2 Hospitalization

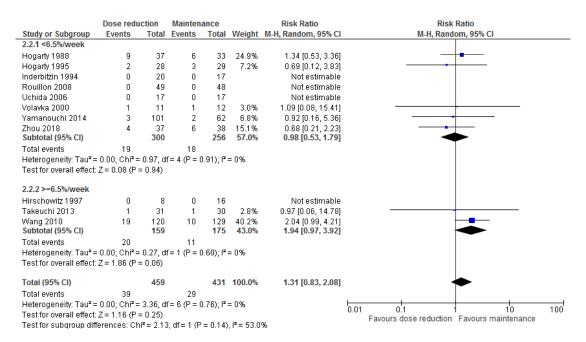


2. Study discontinuation

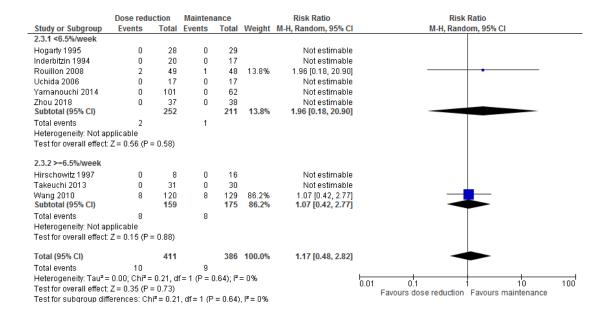
2.1 Study discontinuation due to all causes



2.2 Study discontinuation due to inefficacy

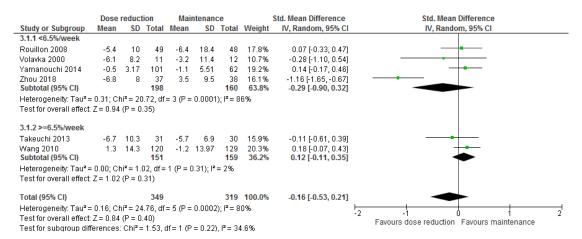


2.3 Study discontinuation due to intolerability

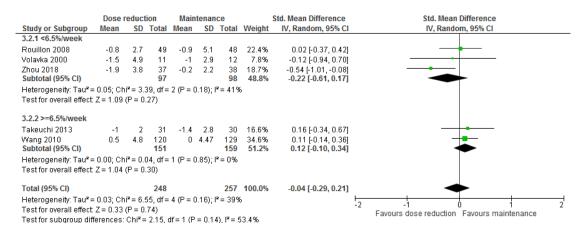


3. Psychopathology

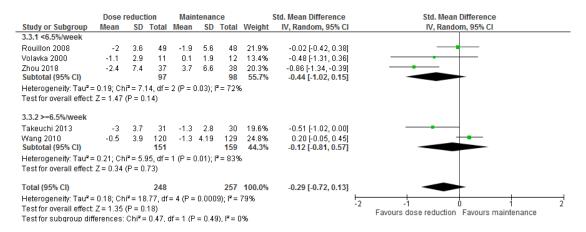
3.1 Total



3.2 Positive symptoms



3.3 Negative symptoms

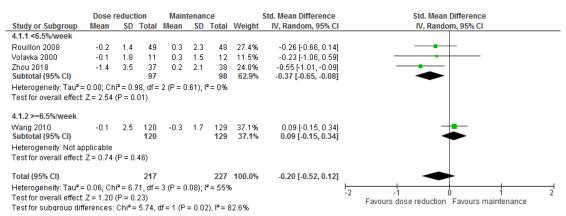


3.4 CGI-S

	Dose	reduct	tion	Main	itenan	ce		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.4.1 <6.5%/week									
Yamanouchi 2014	-0.1	0.55	101	0	1.06	62	34.0%	-0.13 [-0.44, 0.19]	
Subtotal (95% CI)			101			62	34.0%	-0.13 [-0.44, 0.19]	-
Heterogeneity: Not a	pplicable								
Test for overall effect	Z = 0.79	9 (P = 0	.43)						
3.4.2 >=6.5%/week									
Takeuchi 2013	-0.2	0.7	31	0	0.6	30	14.3%	-0.30 [-0.81, 0.20]	
Wang 2010	-0.1	1.1	120	-0.2	1.4	129	51.7%	0.08 [-0.17, 0.33]	-
Subtotal (95% CI)			151			159	66.0%	-0.05 [-0.40, 0.30]	-
Heterogeneity: Tau ² :	= 0.03; C	hi² = 1.	76, df=	1 (P = 0)	0.18); I	² = 439	6		
Test for overall effect	Z = 0.28	6 (P = 0	.80)						
Total (95% CI)			252			221	100.0%	-0.05 [-0.24, 0.15]	•
Heterogeneity: Tau ² :	= 0.00; C	hi² = 2.	21, df=	2 (P = 0	0.33); (²= 9%			1- 1 - 1 - 1
Test for overall effect	Z = 0.48	6(P = 0)	.65)	-					-2 -1 0 1 2 Favours dose reduction Favours maintenance
Test for subgroup dif	ferences	: Chi²=	0.11.	df = 1 (P	= 0.74	4), $J^2 = 0$	1%		Favours dose reduction - Favours maintenance

4. Adverse effects

4.1 SAS



4.2 BARS

	Dose r	Dose reduction Maintenance						Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI		
4.2.1 <6.5%/week												
Rouillon 2008 Subtotal (95% CI)	0.02	1.2	49 49	-0.04	1.6	48 48	100.0% 100.0%	0.04 [-0.36, 0.44] 0.04 [-0.36, 0.44]				
Heterogeneity: Not ap	pplicable											
Test for overall effect:	Z = 0.21	(P = 0.3)	B4)									
4.2.2 >=6.5%/week												
Subtotal (95% CI)			0			0		Not estimable				
Heterogeneity: Not ap	pplicable											
Test for overall effect:	: Not appli	icable										
Total (95% CI)			49			48	100.0%	0.04 [-0.36, 0.44]		-		
Heterogeneity: Not ap Test for overall effect: Test for subgroup diff	Z= 0.21	`		le					-2	-1 0 :	ㅓ 2	

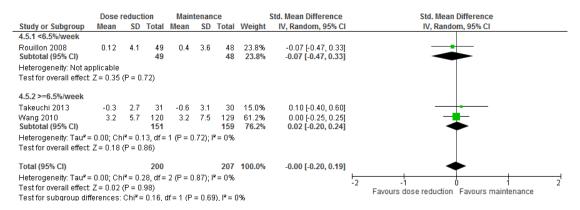
4.3 AIMS

	Dose r	educt	ion	Main	tenan	ice		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.3.1 <6.5%/week									
Rouillon 2008 Subtotal (95% CI)	-0.1	1.6	49 49	-0.4	1.7	48 48	100.0% 100.0 %	0.18 [-0.22, 0.58] 0.18 [-0.22, 0.58]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.89 ((P = 0.	.38)						
4.3.2 >= 6.5%/week Subtotal (95% CI)			0			0		Not estimable	
Heterogeneity: Not ap	•					·		Not estimable	
Test for overall effect:	Not appli	icable							
Total (95% CI) Heterogeneity: Not ap	nlicabla		49			48	100.0%	0.18 [-0.22, 0.58]	
Test for overall effect: Test for subgroup diff	Z = 0.89 (`		le					-2 -1 0 1 2 Favours dose reduction Favours maintenance

4.4 DIEPSS

	Dose	reduct	ion	Main	tenan	ce	Std. Mean Difference			Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
4.4.1 <6.5%/week											
Yamanouchi 2014 Subtotal (95% CI)	-0.69	2.48	101 101	-0.18	4.9	62 62	57.8% 57.8%	-0.14 [-0.46, 0.18] - 0.14 [-0.46, 0.18]		-	
Heterogeneity: Not a	pplicable										
Test for overall effect	Z= 0.87	(P = 0	.38)								
4.4.2 >=6.5%/week											
Takeuchi 2013 Subtotal (95% CI)	-0.9	1.7	31 31	0.1	1.2	30 30	42.2% 42.2%	-0.67 [-1.19, -0.15] - 0.67 [-1.19, -0.15]			
Heterogeneity: Not a	nnlicable		-					,,			
Test for overall effect			.01)								
Total (95% CI)			132			92	100.0%	-0.36 [-0.87, 0.15]			
Heterogeneity: Tau² = 0.09; Chi² = 2.91, df = 1 (P = 0.09); l² = 66% Test for overall effect: Z = 1.40 (P = 0.16)									-2	-1 0 1	2
Test for subgroup differences: Chi ² = 2.91, df = 1 (P = 0.09), I ² = 65.7%										Favours dose reduction Favours maintenance	

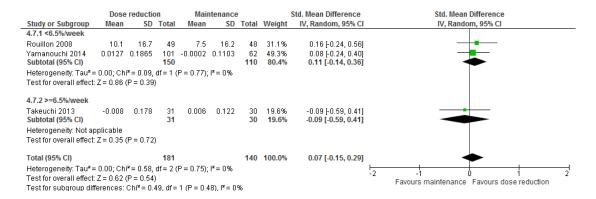
4.5 Body weight



4.6 Neurocognition

	Dose	reduct	ion	Maintenance				Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
4.6.1 <6.5%/week											
Zhou 2018	9.8	13.7	37	3.6	11.5	38	54.6%	0.49 [0.03, 0.95]			
Subtotal (95% CI)			37			38	54.6%	0.49 [0.03, 0.95]			
Heterogeneity: Not ap	oplicable										
Test for overall effect:	Z = 2.07	(P = 0	.04)								
4.6.2 >=6.5%/week											
Takeuchi 2013	7	7.1	31	-0.1	8	30	45.4%	0.93 [0.40, 1.46]			
Subtotal (95% CI)			31		_	30	45.4%	0.93 [0.40, 1.46]			
Heterogeneity: Not as	plicable										
Test for overall effect:	Z= 3.43	(P = 0)	.0006)								
Total (95% CI)			68			68	100.0%	0.69 [0.25, 1.12]	-		
Heterogeneity: Tau ² =	: 0.03: CH	$ni^2 = 1.5$	52. df=	1 (P = 0	0.22):1	² = 349	6		<u> </u>		
Test for overall effect:					//				-2 -1 0 1		
Test for subgroup diff		•		Nf = 1 /D	- 0.21	0) IZ = 0	0.4.406		Favours maintenance Favours dose reduction		

4.7 QOL



Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; CGI-S, Clinical Global Impressions – Severity scale; DIEPSS, Drug-Induced Extrapyramidal Symptoms Scale; QOL, quality of life; SAS, Simpson-Angus Scale